2   Docket No. GJE-59
                                        Serial No. 09/786,015

In the Claims

1 (currently amended):   A non-mutated naturally-occurring high-affinity monoclonal antibody, having a binding affinity to a protein antigen, wherein the affinity is characterisable by:

(i) incubating first and second samples of the antibody in antigen-coated microtitre plate wells at a concentration chosen to be within the linear part of a standard curve at pH 7.2 for 1 hour at 37°C;

(ii) removing unbound antibody from both samples;

(iii) incubating the first sample with PBS at pH 7.2 for 1 hour at 37°C, and reducing the pH of the second sample to pH 3 or below and incubating for 1 hour at 37°C;

(iv) removing unbound antibody from both samples;

(v) incubating both samples with anti-antibody alkaline phosphatase-conjugate for 1 hour at 37°C;

(vi) removing unbound conjugate from both samples; and

(vii) adding PNPP substrate to the samples, measuring the absorbance of the samples at 405 nm, and determining the amount of antibody bound to antigen, wherein the amount bound in the second sample is > 50% of that of the first sample.

2 (currently amended): The antibody, according to claim 1, wherein the amount of antibody bound in the second sample, at the end of step vii, is > 60% of that bound in the first sample.

3 (previously amended): The antibody, according to claim 1, wherein the pH in step (iii) is reduced to pH 2.5 - pH 2.0.

4 (previously amended): The antibody, according to claim 1, which is non-rodent.

5 (currently amended): The antibody, according to claim 1, which has affinity for a tumor-associated antigen.

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6 (previously amended):   The antibody, according to claim 5, wherein the antigen is carcinoembryonic antigen.

7 (previously amended):   The antibody, according to claim 1, which is a single-chain Fv, F(ab')₂, Fv or fab.

8 (currently amended):   The antibody, according to claim 7, having a heavy chain variable region comprising the amino acid sequence defined in SEQ ID No. 2 and a light chain variable region comprising the amino acid sequence defined in SEQ ID No. 4, or a variant thereof ~~having at least the same properties determined by the steps defined in claim 1~~; wherein the binding affinity to a protein antigen of said variant is characterisable by:

(i) incubating first and second samples of the antibody in antigen-coated microtitre plate wells at a concentration chosen to be within the linear part of a standard curve at pH 7.2 for 1 hour at 37°C;

(ii) removing unbound antibody from both samples;

(iii) incubating the first sample with PBS at pH 7.2 for 1 hour at 37°C, and reducing the pH of the second sample to pH 3 or below and incubating for 1 hour at 37°C;

(iv) removing unbound antibody from both samples;

(v) incubating both samples with anti-antibody alkaline phosphatase-conjugate for 1 hour at 37°C;

(vi) removing unbound conjugate from both samples; and

(vii) adding PNPP substrate to the samples, measuring the absorbance of the samples at 405 nm, and determining the amount of antibody bound to antigen, wherein the amount bound in the second sample is > 50% of that of the first sample.

9 (withdrawn)

10 (withdrawn)

11 (new): A high-affinity monoclonal antibody, wherein said antibody is a natural antibody produced by immunizing a non-rodent mammal with a protein antigen, or is a recombinantly-produced version of said natural antibody, and wherein the affinity of said antibody is characterisable by:

(i) incubating first and second samples of the antibody in antigen-coated microtitre plate wells at a concentration chosen to be within the linear part of a standard curve at pH 7.2 for 1 hour at 37°C;

(ii) removing unbound antibody from both samples;

(iii) incubating the first sample with PBS at pH 7.2 for 1 hour at 37°C, and reducing the pH of the second sample to pH 3 or below and incubating for 1 hour at 37°C;

(iv) removing unbound antibody from both samples;

(v) incubating both samples with anti-antibody alkaline phosphatase-conjugate for 1 hour at 37°C;

(vi) removing unbound conjugate from both samples; and

(vii) adding PNPP substrate to the samples, measuring the absorbance of the samples at 405 nm, and determining the amount of antibody bound to antigen, wherein the amount bound in the second sample is > 50% of that of the first sample.

12 (new): The antibody, according to claim 11, wherein the amount of antibody bound in the second sample, at the end of step vii, is > 60% of that bound in the first sample.

13 (new): The antibody, according to claim 11, wherein the pH in step (iii) is reduced to pH 2.5 - pH 2.0.

14 (new): The antibody, according to claim 11, which is non-rodent.

15 (new): The antibody, according to claim 11, which has affinity for a tumor-associated antigen.

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16 (new): The antibody, according to claim 15, wherein the antigen is carcinoembryonic antigen.

17 (new): The antibody, according to claim 11, which is a single-chain Fv, F(ab')$_2$, Fv or fab.

18 (new): The antibody, according to claim 17, having a heavy chain variable region comprising the amino acid sequence defined in SEQ ID No. 2 and a light chain variable region comprising the amino acid sequence defined in SEQ ID No. 4, or a variant thereof; wherein the binding affinity of said variant to a protein antigen is characterisable by:

(i) incubating first and second samples of the antibody in antigen-coated microtitre plate wells at a concentration chosen to be within the linear part of a standard curve at pH 7.2 for 1 hour at 37°C;

(ii) removing unbound antibody from both samples;

(iii) incubating the first sample with PBS at pH 7.2 for 1 hour at 37°C, and reducing the pH of the second sample to pH 3 or below and incubating for 1 hour at 37°C;

(iv) removing unbound antibody from both samples;

(v) incubating both samples with anti-antibody alkaline phosphatase-conjugate for 1 hour at 37°C;

(vi) removing unbound conjugate from both samples; and

(vii) adding PNPP substrate to the samples, measuring the absorbance of the samples at 405 nm, and determining the amount of antibody bound to antigen, wherein the amount bound in the second sample is > 50% of that of the first sample.